

U.S.S.N. 09/760,362
CHEN
AMENDMENT

AMENDMENTS TO THE SPECIFICATION

Please insert paragraph [000.1] before paragraph [001] on page 1:

RELATED APPLICATIONS

[000.1] This application claims benefit of U.S. Application Ser. No. 60/175,689, filed January 12, 2000. This application is also related to the PCT application PCT/US01/00922, entitled "Novel Treatment for Eye Disease," Inventor James C. Chen, filed on even date herewith. Each of these applications is incorporated by reference herein in its entirety as if fully set forth below.

Please replace paragraph [021] with the following paragraph:

[021] Yet another preferred embodiment contemplates a method of PDT of neovascular disease of the eye as described above, where the ligand is selected from the group consisting of: VEGF; VEGF receptor; and $\alpha v \beta 3$ ~~$\alpha 3, \beta 3$~~ integrin receptor. A further preferred embodiment provides a method of PDT of neovascular disease of the eye, where the ligand comprises an antibody specific or having a high degree of affinity for the extra-domain B (or ED-B) of fibronectin. An even more preferred embodiment is drawn to the ligand discussed above, which is a complete or functional bindable fragment of a human antibody, such as L19 or its equivalent (see Birchler *et al.*, *Selective targeting and photocoagulation of ocular angiogenesis mediated by a phage-derived human antibody fragment*, *Nature Biotech.* 17:984 (1999)).

Please replace paragraph [042] with the following paragraph:

[042] The photosensitizing compound is administered orally, intravenously by injection, or via the intraocular route. The photosensitizing compound can be conjugated to various antibodies, antibody fragments, and other molecules and compounds capable of binding the endothelium of neovessels. The specific ligands reactive with the target endothelium include antibodies and antibody

such as the $\alpha v \beta 3$ integrin receptor (see Birchler *et al.*, *Microbiol Immunol*, 237:1-30, 1999; Elicieri and Cheresh, *The Journal of Clinical*

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Investigation, 103:1227-30, 1999; Smith *et al.*, *Br J Opthamol*, 83:486-494, 1999). Also, the antibody can be drawn to and have affinity to bind to the extra-domain B (or ED-B) of fibronectin. Such antibodies, include a complete or functional bindable fragment of a human antibody, such as L19 or its equivalent (see: Birchler *et al.*, *Selective targeting and photocoagulation of ocular angiogenesis mediated by a phage-derived human antibody fragment*, *Nature Biotech.* 17:984 (1999)). The ligand can be any molecule or compound that binds to a endothelial receptor found on an abnormal blood vessel wall. Preferably the ligand binds selectively to receptors which are mainly or only found on the abnormal blood vessel wall.

Please replace paragraph [061] with the following paragraph:

[061] ~~Integrin~~ $\alpha v \beta 3$ integrin is expressed by vascular cells during angiogenesis and vascular remodeling and is highly expressed by endothelial cells undergoing angiogenesis in tumors. See Eliceiri, B.P. *et al.* *J. Clin. Invest* (1999) 103(9):1227-1230. Antibody elicited to $\alpha v \beta 3$, such as LM609 (Vitaxin; Eliceiri *et al.*) is conjugated to a texaphyrin photosensitizing agent in a liposomal formulation. A drug does of 25 mg/m² is administered via intravenous infusion over 10 min. The photosensitizer localizes to the neovascular ~~neovascuature~~ lesions. The pupils are dilated to allow ambient light enter for photosensitization. Therefore, no slit lamp is needed for photosensitization and the subject may continue everyday activities while receiving PDT. The ambient light is used to photoactivate the photosensitizing agent for a total exposure time of 24 hours.